COVID-19 and ABO blood group: another viewpoint

Li *et al.*[1] have recently published '*Association between ABO blood groups and risk of SARS-CoV-2 pneumonia*', an observation already reported a few weeks ago as a MedRxiv preprint by Zhao *et al.*[2] and which had a certain impact in the press.

In both studies, the ABO blood groups distribution of patients with coronavirus disease 2019 (COVID-19) were compared to that of controls from the local populations that showed that blood group A was associated with an increased risk of infection, whereas group O was associated with a decreased risk. Considering this information rather as a working hypothesis, some scientists have called for caution.[3]

However, as already strongly suggested by others,[4] this variable susceptibility to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection could be linked to circulating anti-A antibodies, which could interfere or even inhibit the virus–cell adhesion process.

We had the idea to analyse these important available data series from the anti-A or -B antibodies viewpoint instead of ABO blood group antigens as the authors did.

In fact, considering the largest series of patients with COVID-19 ($N = 1888$) analysed by Zhao *et al.*,[2] we compared the proportion of those possessing anti-A in their serum (i.e. those of B and O blood groups) and those who did not (i.e. those of A and AB blood groups) to the control cohort ($N = 3694$; Table I).

The results (Table I) indicate that subjects with anti-A in serum (i.e. B and O blood groups) are significantly less represented in the COVID-19 group than those lacking anti-A whatever the group: A and AB ($P < 0{\cdot}001$), A ($P < 0{\cdot}001$) or AB ($P = 0{\cdot}0323$), whereas there was no significant difference *versus* circulating anti-B (data not shown).

We then wondered if there was a difference between anti-A from O and anti-A from B, and then we compared the supposed protective effect of anti-A from O and from B (Table II).

Whereas both blood group O and B patients possess circulating seric anti-A, it appears and it is statistically highly significant ($P < 0{\cdot}001$) that O group patients are underrepresented (49·4 % vs. 57·6%), whereas B group patients are, on the contrary, overrepresented (50·6% vs. 42·4%), meaning that anti-A from O is more protective than anti-A from B.

This latter observation is probably related to the fact that the immunoglobulin predominant isotype of anti-B/anti-A is IgM in serum from group A and B individuals, but IgG in O group serum, an already known notion,[5] which has been well documented by flow cytometry.[6]

In conclusion, this way of analysing the data strongly suggests that the presence of anti-A antibodies in serum and more specifically IgG anti-A, should be considered as a factor more significant than the blood group itself, as far as the relationship between COVID-19 susceptibility and ABO blood groups is concerned.

Far from intending to corroborate the authors' conclusions as such, we wanted to show that the resources of immuno-haematology allow several approaches that could perhaps be useful for the disease follow-up.

Table I. Comparison of subjects with/without anti-A antibodies in their serum.

	RBC blood group	Control, *n* (%)	COVID-19, *n* (%)	χ^2	*P*	OR (95% CI)
With anti-A	B and O	2170 (58·7)	927 (52·2)			
	A and AB	1524 (41·3)	848 (47·8)	20·74	<0·001	1·30 (1·16–1·46)
Without anti-A	A	1188 (32·2)	670 (37·7)	19·97	<0·001	1·32 (1·17–1·49)
	AB	336 (9·1)	178 (10·0)	4·58	0·0323	1·24 (1·02–1·51)

Table II. Comparison of anti-A from O and from B subjects.

	RBC blood group	Control, *n* (%)	COVID-19, *n* (%)	χ^2	*P*	OR (95% CI)
Anti-A from O	O	1250 (57·6)	458 (49·4)			
Anti-A from B	B	920 (42·4)	469 (50·6)	17·64	<0·001	1·39 (1·19–1·62)

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